

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
13 July 2006 (13.07.2006)

PCT

(10) International Publication Number
WO 2006/072809 A2

(51) International Patent Classification: Not classified

(21) International Application Number: PCT/IB2004/004472

(22) International Filing Date: 29 October 2004 (29.10.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/515,648 31 October 2003 (31.10.2003) US
60/573,339 25 May 2004 (25.05.2004) US
60/624,625 25 October 2004 (25.10.2004) US

(71) Applicant (for all designated States except US): RO-BARTS RESEARCH INSTITUTE [CA/CA]; 100 Perth Drive, P.O. Box 5015, London, Ontario N6A 5K8 (CA).

(72) Inventors; and

(75) Inventors/Applicants (for US only): PICKERING, John, Geoffrey [CA/CA]; 26 Masonville Cres, London, Ontario N5X 3T2 (CA). VAN DER VEER, Eric, Peter [CA/CA]; 320 Hyman Street, London, Ontario N6B 2G7 (CA).

(74) Agent: DEETH WILLIAMS WALL LLP; 150 York Street, Suite 400, Toronto, Ontario M5H 3S5 (CA).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

[Continued on next page]

(54) Title: METHODS AND FORMULATIONS FOR PROTECTING CELLS, AND FOR TREATING DISEASES AND CONDITIONS BY OPTIMIZING THE INTRACELLULAR CONCENTRATION OF NAD

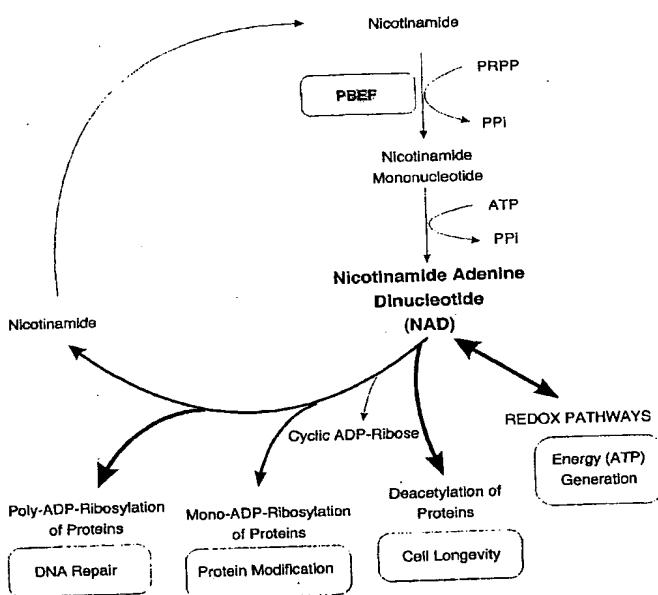


Figure Utilization and Regeneration of NAD
NAD is essential for redox pathways including oxidative phosphorylation, but these do not consume NAD. In contrast, NAD is consumed during vital cellular reactions such as DNA repair, protein modification, generating the signaling molecule cADP ribose, and NAD-dependent deacetylation of proteins. Maintenance of these reactions requires resynthesis of NAD from nicotinamide (salvage). PBEP is the rate-limiting enzyme for this salvage pathway.

WO 2006/072809 A2

(57) Abstract: Pharmaceutical and cosmetic formulations and methods for optimizing the intracellular concentrations of NAD are provided. The present methods and compounds relate to the use of PBEP, PRPP and various forms of nicotinamide, individually or in combination, for therapeutic, cyto-protective, cosmetic and anti-aging purposes. PBEP, PRPP and nicotinamide, individually or in combination, as administered according to the invention, increase the metabolic fitness, health and performance of the cell, and thereby increase the cell's level of health during its lifecycle. By way of the present formulations and methods, optimizing the intracellular concentration of NAD⁺ facilitates a balance among the numerous intracellular interactions of NAD⁺, and its related pathways, such that the health of the cell and its resistance to stress and trauma are increased. This increased robustness attendant to the invention also facilitates the delay of apoptosis.